

R^1 is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

R^2 is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

wherein Ph denotes a phenyl group which is optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from a C₁₋₄ alkyl group, -F, -Cl, -Br, -I, -CN, or -NO₂;

R^{1a} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group;

R^{2a} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group;

R^{1b} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group;

R^{2b} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group;

R^3 is -F, -Cl, -Br, -I, -OCHF₂, -C≡CH, -OCF₃, -CH₃, -CF₃, -SF₅, -SCF₃, or -CF₂CF₃;

R^4 is -H, -F, -Cl, -Br, -I, -OCHF₂, -C≡CH, -OCF₃, -CH₃, -CF₃, -SF₅, -SCF₃, or -CF₂CF₃;

R^5 is -H or -F;

with the proviso that if R^4 is -H, then R^3 is not -F;

R^7 is -H, -C(CH₃)₃, or -CH₂-CH=CH₂;

Z is -CH₂-T-W;

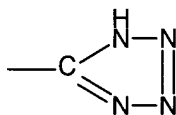
T is -CH₂-, -O-, -S-, -(S=O)-, or -(SO₂)-;

the group -CH₂-T- may optionally be substituted with 1 or 2 substituents, denoted Q¹ and Q² respectively, on carbon, wherein Q¹ and Q² are independently a C₁₋₄alkyl group or a halogen; or, when Q¹ and Q² are bonded to adjacent carbon atoms, Q¹ and

Q² together may form a C₃₋₄alkylene radical optionally substituted with 1, 2, 3 or 4 substituents independently selected from C₁₋₄alkyl groups and halogens;

W is one of:

- (1) -COOH ;
- (2) -(C=O)OR⁸ ;
- (3) -(C=O)NR⁹R⁹ ;
- (4) -SO₂NHR¹⁰ ;
- (5) -SO₂OR¹¹ ;
- (6) -PO₃R¹¹R¹¹ ;
- (7) a tetrazol-5-yl group:



- (8) -CONH-SO₂R¹² ; and,
- (9) -M-Het;

with the proviso that if T is -O-, -S-, -(S=O)-, or -(SO₂)-, then W is not -COOH;

wherein:

R⁸ is a C₁₋₆alkyl group, a C₃₋₆cycloalkyl group, a C₅₋₂₀aryl group, or -CH₂-CH=CH₂ ;

wherein the C₅₋₂₀aryl group may optionally be substituted on carbon with from 1 to 4 substituents selected from -COOH, -OH, -NH₂, -CH₂NH₂, -(CH₂)₁₋₄COOH, tetrazol-5-yl, and -SO₃H;

R^9 is independently -H, a C_{1-6} alkyl group, a C_{3-6} cycloalkyl group, a C_{5-20} aryl group, a C_{7-9} aralkyl group, or a C_{5-20} heteroaryl group linked to N via carbon;

wherein the C_{5-20} aryl group, the C_{5-20} heteroaryl group, and aryl moiety of the C_{7-9} aralkyl group may optionally be substituted on carbon with from 1 to 4 substituents selected from -COOH, -OH, -NH₂, -CH₂NH₂, -(CH₂)₁₋₄COOH, tetrazol-5-yl, and -SO₃H;

and wherein the C_{3-6} cycloalkyl group may optionally carry a methyl group;

R^{10} is a C_{1-6} alkyl group, -CH₂-CH=CH₂, a C_{3-6} cycloalkyl group, a C_{1-4} haloalkyl group (e.g., -CF₃, -CH₂CF₃), or a C_{5-20} aryl group;

wherein the C_{5-20} aryl group, the C_{5-20} heteroaryl group, and aryl moiety of the C_{7-9} aralkyl group may optionally be substituted on carbon with from 1 to 4 substituents selected from -COOH, -OH, -NH₂, -CH₂NH₂, -(CH₂)₁₋₄COOH, tetrazol-5-yl, and -SO₃H;

and wherein the C_{3-6} cycloalkyl group may optionally carry a methyl group;

R^{11} represents -H, a C_{1-6} alkyl group, or a C_{3-6} cycloalkyl group;

R^{12} is one of:

- (a) a C_{3-7} cycloalkyl group;
- (b) a C_{1-6} alkyl group, optionally substituted with one or more of: a phenyl group; a phenyl group with from 1 to 5 substituents selected from halogen, -NO₂, -CF₃, C_{1-4} alkyl, C_{1-4} alkoxy, -NH₂, -NHCOCH₃, -CONH₂, -OCH₂COOH, -NH(C_{1-4} alkyl), -N(C_{1-4} alkyl)₂, -NHCOOC C_{1-4} alkyl, -OH, -COOH, -CN and -COOC C_{1-4} alkyl; a C_{1-4} alkyl group; a C_{1-4} haloalkyl group; or a halogen; and,

(c) a C_{1-6} perfluoroalkyl group;

M represents -S-, -SO-, or -SO₂-; and,

Het represents a 5 or 6 membered heterocyclic aromatic ring linked to M via a carbon atom of the aromatic ring, said aromatic ring containing 1, 2, 3 or 4 heteroatoms selected from the group consisting of O, N and S said aromatic ring optionally being substituted on carbon atoms of the ring with 1, 2, 3 or 4 substituents selected from the group consisting of -OH, -SH, -CN, -CF₃, NH₂ and halogen.

49. (new) A compound according to claim 48, wherein:

R¹ and R² are independently -I, -Br, or -Cl.

50. (new) A compound according to claim 48, wherein: R¹ and R² are both -I.

51. (new) A compound according to claim 48, wherein:

R^{1a}, R^{1b}, R^{2a}, R^{2b} are each independently -H or -CH₃.

52. (new) A compound according to claim 48, wherein:

R^{1a}, R^{1b}, R^{2a}, R^{2b} are each independently -H or -CH₃.

53. (new) A compound according to claim 48, wherein: R^{1a}, R^{1b}, R^{2a}, R^{2b} are all -H.

54. (new) A compound according to claim 49, wherein: R^{1a}, R^{1b}, R^{2a}, R^{2b} are all -H.

55 (new) A compound according to claim 50, wherein: R^{1a} , R^{1b} , R^{2a} , R^{2b} are all -H.

56. (new) A compound according to claim 48, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; or,
- (b) R^3 and R^4 are both -F.

57. (new) A compound according to claim 49, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; or,
- (b) R^3 and R^4 are both -F.

58. (new) A compound according to claim 50, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; or,
- (b) R^3 and R^4 are both -F.

59. (new) A compound according to claim 54, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; or,
- (b) R^3 and R^4 are both -F.

60. (new) A compound according to claim 55, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; or,

(b) R^3 and R^4 are both -F.

61. (new) A compound according to claim 48, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; and, R^5 is -H; or,
- (b) R^3 and R^4 are both -F; and, R^5 is -F; or,
- (c) R^3 and R^4 are both -F; and, R^5 is -H.

62. (new) A compound according to claim 49, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; and, R^5 is -H; or,
- (b) R^3 and R^4 are both -F; and, R^5 is -F; or,
- (c) R^3 and R^4 are both -F; and, R^5 is -H.

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63. (new) A compound according to claim 50, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; and, R^5 is -H; or,
- (b) R^3 and R^4 are both -F; and, R^5 is -F; or,
- (c) R^3 and R^4 are both -F; and, R^5 is -H.

64. (new) A compound according to claim 54, wherein:

- (a) R^3 and R^4 are $-CF_3$ and -H, respectively; and, R^5 is -H; or,
- (b) R^3 and R^4 are both -F; and, R^5 is -F; or,
- (c) R^3 and R^4 are both -F; and, R^5 is -H.

65. (new) A compound according to claim 55, wherein:

- (a) R^3 and R^4 are $-CF_3$ and $-H$, respectively; and, R^5 is $-H$; or,
- (b) R^3 and R^4 are both $-F$; and, R^5 is $-F$; or,
- (c) R^3 and R^4 are both $-F$; and, R^5 is $-H$.

66. (new) A compound according to claim 48, wherein:

Z is $-CH_2-T-C(=O)OH$ or $-CH_2-T-C(=O)OR^8$; and, T is $-CH_2-$.

67. (new) A compound according to claim 49, wherein:

Z is $-CH_2-T-C(=O)OH$ or $-CH_2-T-C(=O)OR^8$; and, T is $-CH_2-$.

68. (new) A compound according to claim 50, wherein:

Z is $-CH_2-T-C(=O)OH$ or $-CH_2-T-C(=O)OR^8$; and, T is $-CH_2-$.

69. (new) A compound according to claim 54, wherein:

Z is $-CH_2-T-C(=O)OH$ or $-CH_2-T-C(=O)OR^8$; and, T is $-CH_2-$.

70. (new) A compound according to claim 55, wherein:

Z is $-CH_2-T-C(=O)OH$ or $-CH_2-T-C(=O)OR^8$; and, T is $-CH_2-$.

71. (new) A compound according to claim 56, wherein:

Z is $-CH_2-T-C(=O)OH$ or $-CH_2-T-C(=O)OR^8$; and, T is $-CH_2-$.

72. (new) A compound according to claim 61, wherein:

Z is $-\text{CH}_2\text{-T-C(=O)OH}$ or $-\text{CH}_2\text{-T-C(=O)OR}^8$; and, T is $-\text{CH}_2-$.


73. (new) A compound according to claim 62, wherein:

Z is $-\text{CH}_2\text{-T-C(=O)OH}$ or $-\text{CH}_2\text{-T-C(=O)OR}^8$; and, T is $-\text{CH}_2-$.

74. (new) A compound according to claim 63, wherein:

Z is $-\text{CH}_2\text{-T-C(=O)OH}$ or $-\text{CH}_2\text{-T-C(=O)OR}^8$; and, T is $-\text{CH}_2-$.

75. (new) A compound according to claim 66, wherein: R^8 is $-\text{H}$, $-\text{C}(\text{CH}_3)_3$, or

 $-\text{CH}_2\text{-CH=CH}_2$.

76. (new) A compound according to claim 67, wherein: R^8 is $-\text{H}$, $-\text{C}(\text{CH}_3)_3$, or

$-\text{CH}_2\text{-CH=CH}_2$.

77. (new) A compound according to claim 68, wherein: R^8 is $-\text{H}$, $-\text{C}(\text{CH}_3)_3$, or

$-\text{CH}_2\text{-CH=CH}_2$.

78. (new) A compound according to claim 69, wherein: R^8 is $-\text{H}$, $-\text{C}(\text{CH}_3)_3$, or

$-\text{CH}_2\text{-CH=CH}_2$.

79. (new) A compound according to claim 70, wherein: R^8 is -H, $-C(CH_3)_3$, or $-CH_2-CH=CH_2$.

80. (new) A compound according to claim 71, wherein: R^8 is -H, $-C(CH_3)_3$, or $-CH_2-CH=CH_2$.

81. (new) A compound according to claim 72, wherein: R^8 is -H, $-C(CH_3)_3$, or $-CH_2-CH=CH_2$.

82. (new) A compound according to claim 73, wherein: R^8 is -H, $-C(CH_3)_3$, or $-CH_2-CH=CH_2$.

83. (new) A compound according to claim 74, wherein: R^8 is -H, $-C(CH_3)_3$, or $-CH_2-CH=CH_2$.

84. (new) A compound selected from:

{3,5-difluoro-4-[bis(2-iodoethyl)amino]benzoyl}-L-glutamic acid;

{3,5-difluoro-4-[bis(2-chloroethyl)amino]benzoyl}-L-glutamic acid;

{3,5-difluoro-4-[bis(2-bromoethyl)amino]benzoyl}-L-glutamic acid;

{2,3,5-trifluoro-4-[bis(2-chloroethyl)amino] benzoyl}-L-glutamic acid;

{2,3,5-trifluoro-4-[bis(2-bromoethyl)amino]benzoyl}-L-glutamic acid;

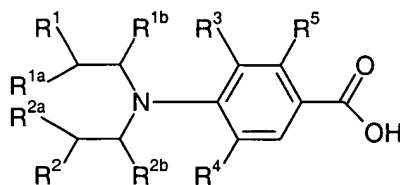
{2,3,5-trifluoro-4-[bis(2-iodoethyl)amino]benzoyl}-L-glutamic acid;

{3,5-difluoro-4-[bis(2-bromopropyl)amino] benzoyl}-L-glutamic acid;
{3-trifluoromethyl-4-[bis(2-bromoethyl)amino] benzoyl}-L-glutamic acid; and,
the di-*tert*-butyl esters thereof.

85. (new) A compound selected from:

{3,5-difluoro-4-[bis(2-iodoethyl)amino]benzoyl}-L-glutamic acid;
and, the di-*tert*-butyl ester thereof.

86. (new) A compound of Formula II:



wherein:

R¹ is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

R² is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

wherein Ph denotes a phenyl group which is optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from a C₁₋₄ alkyl group, -F, -Cl, -Br, -I, -CN, or -NO₂;

R^{1a} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{2a} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{1b} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{2b} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^3 is -F, -Cl, -Br, -I, -OCHF₂, -C≡CH, -OCF₃, -CH₃, -CF₃, -SF₅, -SCF₃, or -CF₂CF₃;

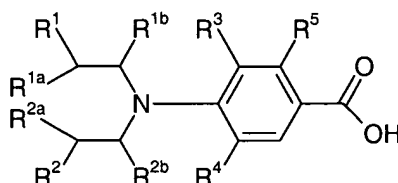
R^4 is -H, -F, -Cl, -Br, -I, -OCHF₂, -C≡CH, -OCF₃, -CH₃, -CF₃, -SF₅, -SCF₃, or -CF₂CF₃;

R^5 is -H or -F;

with the proviso that if R^4 is -H, then R^3 is not -F; and,

with the proviso that if R^1 is -Cl, R^2 is -Cl, R^{1a} is -H, R^{2a} is -H, R^{1b} is -H, R^{2b} is -H, R^4 is -H, and R^5 is -H, then R^3 is not -CH₃.

87. (new) A compound of Formula II:



wherein:

R^1 is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

R^2 is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

wherein Ph denotes a phenyl group which is optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from a C₁₋₄ alkyl group, -F, -Cl, -Br, -I, -CN, or -NO₂;

R^{1a} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{2a} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{1b} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{2b} is -H, a C_{1-4} alkyl group, or a C_{1-4} haloalkyl group ;

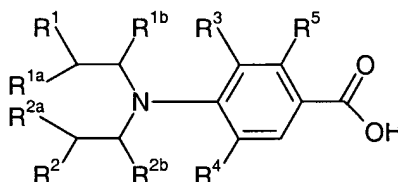
R^3 is -F, -Cl, -Br, -I, -OCHF₂, -C≡CH, -OCF₃, -CF₃, -SF₅, -SCF₃, or -CF₂CF₃ ;

R^4 is -H, -F, -Cl, -Br, -I, -OCHF₂, -C≡CH, -OCF₃, -CF₃, -SF₅, -SCF₃, or -CF₂CF₃ ;

R^5 is -H or -F;

with the proviso that if R^4 is -H, then R^3 is not -F.

88. (new) A compound of Formula II:



wherein:

R^1 is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

R^2 is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

wherein Ph denotes a phenyl group which is optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from a C_{1-4} alkyl group, -F, -Cl, -Br, -I, -CN, or -NO₂;

R^{1a} is -H, a C_{1-4} alkyl group, or a C_{1-4} haloalkyl group ;

R^{2a} is -H, a C_{1-4} alkyl group, or a C_{1-4} haloalkyl group ;

R^{1b} is -H, a C_{1-4} alkyl group, or a C_{1-4} haloalkyl group ;

R^{2b} is -H, a C_{1-4} alkyl group, or a C_{1-4} haloalkyl group ;

R^3 and R^4 are -CF₃ and -H, respectively,

or R^3 and R^4 are both -F; and

R^5 is -H or -F.

89. (new) A compound according to claim 86, wherein: R^1 and R^2 are independently -I, -Br, or -Cl.

90. (new) A compound according to claim 86, wherein: R^1 and R^2 are both -I.

91. (new) A compound according to claim 86, wherein:

R^{1a} , R^{1b} , R^{2a} , R^{2b} are each independently -H or -CH₃.

92. (new) A compound according to claim 86, wherein: R^{1a} , R^{1b} , R^{2a} , R^{2b} are all

-H.

93. (new) A compound according to claim 86, wherein:

(a) R^3 and R^4 are -CF₃ and -H, respectively; or,

(b) R^3 and R^4 are both -F.

94. (new) A compound according to claim 86, wherein:

(a) R^3 and R^4 are -CF₃ and -H, respectively; and, R^5 is -H; or,

(b) R^3 and R^4 are both -F; and, R^5 is -F; or,

(c) R^3 and R^4 are both -F; and, R^5 is -H.

95. (new) A compound according to claim 86 selected from:

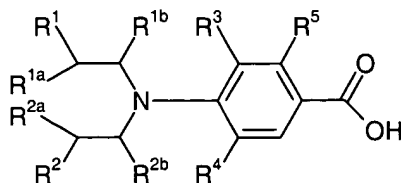
3,5-difluoro-4-[bis(2-iodoethyl)amino]benzoic acid;
3,5-difluoro-4-[bis(2-chloroethyl)amino]benzoic acid;
3,5-difluoro-4-[bis(2-bromoethyl)amino]benzoic acid;
2,3,5-trifluoro-4-[bis(2-chloroethyl)amino]benzoic acid;
2,3,5-trifluoro-4-[bis(2-bromoethyl)amino]benzoic acid;
2,3,5-trifluoro-4-[bis(2-iodoethyl)amino]benzoic acid;
3,5-difluoro-4-[bis(2-bromopropyl)amino]benzoic acid; and,
3-trifluoromethyl-4-[bis(2-bromoethyl)amino]benzoic acid.

96. (new) A composition comprising a compound according to claim 48, and a pharmaceutically acceptable carrier or diluent.

97. (new) A composition comprising a compound according to claim 86, and a pharmaceutically acceptable carrier or diluent.

98. (new) A two-component system comprising:

(i) a first component capable of delivering a carboxypeptidase enzyme to the interior or exterior of a target cell or a vector encoding said enzyme to the interior of said cell such that said vector expresses said enzyme in said cell, and
(ii) a prodrug of according to claim 48 capable of being converted by said enzyme into a compound of Formula II:



wherein:

R^1 is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

R^2 is -Cl, -Br, -I, -OSO₂CH₃, or -OSO₂Ph ;

wherein Ph denotes a phenyl group which is optionally substituted with 1, 2, 3, 4 or 5 substituents independently selected from a C₁₋₄ alkyl group, -F, -Cl, -Br, -I, -CN, or -NO₂;

R^{1a} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{2a} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{1b} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^{2b} is -H, a C₁₋₄alkyl group, or a C₁₋₄haloalkyl group ;

R^3 is -F, -Cl, -Br, -I, -OCHF₂, -C≡CH, -OCF₃, -CH₃, -CF₃, -SF₅, -SCF₃, or -CF₂CF₃;

R^4 is -H, -F, -Cl, -Br, -I, -OCHF₂, -C≡CH, -OCF₃, -CH₃, -CF₃, -SF₅, -SCF₃, or -CF₂CF₃;

R^5 is -H or -F;

with the proviso that if R^4 is -H, then R^3 is not -F; and,

with the proviso that if R^1 is -Cl, R^2 is -Cl, R^{1a} is -H, R^{2a} is -H, R^{1b} is -H, R^{2b} is -H, R^4 is -H, and R^5 is -H, then R^3 is not -CH₃.

99. (new) A kit comprising:

(a) a compound according to claim 48; and,

(b) one of:

(i) an immunoglobulin/enzyme fusion protein or conjugate in which the immunoglobulin is specific for a cellular antigen and the enzyme is a carboxypeptidase enzyme;

(ii) a ligand/enzyme conjugate or fusion protein, the ligand being specific for a cellular antigen and the enzyme is a carboxypeptidase enzyme;

(iii) a vector which encodes a carboxypeptidase enzyme which can be expressed in a cell.

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100. (new) A method for the treatment of cancer comprising administering to a subject suffering from cancer a therapeutically-effective amount of a compound according to claim 48.

101. (new) A method for the treatment of cancer comprising administering to a subject suffering from cancer a therapeutically-effective amount of a compound according to claim 85.

102. (new) A method for the treatment of cancer comprising administering to a subject suffering from cancer a therapeutically-effective amount of a compound according to claim 86.--